NEJM study points to new era in hepatitis C treatment

June 5 2009

For patients with the most common form of hepatitis C, the addition of a hepatitis C-specific protease inhibitor called telaprevir to the current standard therapy can significantly improve the chances of being cured, and it does it in half the time of standard therapy alone.

Results of the Phase IIb clinical trial -- led by Duke Clinical Research Institute (DCRI) and 36 other sites, including NewYork-Presbyterian Hospital/Weill Cornell Medical Center -- are published in the April 30th issue of the New England Journal of Medicine. The study was funded by Vertex Pharmaceuticals Incorporated, the maker of the drug telaprevir. The drug works by blocking an enzyme that the hepatitis C virus needs in order to replicate itself.

"These findings point the way to a new era in the treatment of hepatitis C," says Dr. Ira M. Jacobson, a co-author of the study and chief of the Division of Gastroenterology and Hepatology at NewYork-Presbyterian Hospital/Weill Cornell Medical Center, and the Vincent Astor Distinguished Professor of Clinical Medicine at Weill Cornell Medical College. "Not only does adding telaprevir make standard hepatitis C treatment more effective, but it makes it work much more quickly. We showed that the duration of therapy can be reduced from 48 weeks to 24 weeks for most patients. This could help reduce the potentially severe side effects of longer regimens with standard therapy."

The randomized, double-blinded trial followed 250 patients with untreated hepatitis C genotype 1. Researchers measured rates of

sustained viral response or viral cure -- an undetectable quantity of hepatitis C virus -- 24 weeks after the end of completion of therapy. They compared a 12-week regimen of telaprevir combined with two different durations of the standard therapy -- peginterferon alfa-2a and ribavirin -- to a control group taking 48 weeks of standard therapy alone. Results showed that 67 percent of patients taking telaprevir in combination with standard therapy for 12 weeks followed by standard therapy alone for 36 weeks were cured; and 61 percent of those taking telaprevir in combination with standard therapy for 12 weeks followed by standard therapy alone for 12 weeks were cured. This is compared to 41 percent cure rate in the 48-week control group.

The study also showed that the percentage of patients who relapsed in the 24-week and 48-week telaprevir-based groups (2 percent and 6 percent, respectively) was much lower than the control group (23 percent).

The most common reported side effect in the telaprevir groups was rash, and contributed to some patients discontinuing the therapy.

Peginterferon alfa-2a is an antiviral drug given by injection that is also used to treat HIV and hepatitis B; it works in conjunction with a drug called ribavirin, a nucleoside analogue, to suppress the viral activity of hepatitis C. Side effects can include severe flu-like symptoms, depression, fatigue, insomnia and anemia.

"Treating genotype 1 hepatitis C, the most common form of the infection in the United States, can be challenging because the side effects are difficult for many people to endure, the duration of treatment is long, and traditionally less than half of patients are able to be cured of their disease," says Dr. Andrew Muir, a gastroenterologist at Duke Clinical Research Institute and a senior investigator on the study. "Even though telaprevir does produce side effects of its own, its addition to

standard therapy was able to improve response rates and shorten the duration of treatment necessary -- either one alone would have been an advance, and to be able to achieve both is a significant step in the right direction when it comes to treating hepatitis C."

The study's lead author is Dr. John McHutchison, a hepatologist and gastroenterologist and researcher at the Duke Clinical Research Institute. Additional co-authors include Drs. Gregory Everson of the University of Colorado Health Science Center; Stuart Gordon of Henry Ford Hospital; Mark Sulkowski of Johns Hopkins School of Medicine; and Robert Kauffman, Lindsay McNair and John Alam of Vertex Pharmaceuticals.

Drs. Jacobson, McHutchison and Muir have received consulting fees and/or grant support from Vertex, Roche (maker of peginterferon) and Schering-Plough (maker of ribavirin).

The study's results match those of a similar study conducted in Europe that was reported on in the same issue of the New England Journal of Medicine. An accompanying editorial recounts the history of hepatitis C treatments, beginning 25 years ago with the discovery of interferon. It comments on the two studies: "Telaprevir appears to be a material advance in the therapy of hepatitis C, beginning a new era of treatment -- an era of antiviral agents developed specifically to target this virus."

Two Phase III studies currently under way at NewYork-Presbyterian/Weill Cornell and centers worldwide will attempt to confirm the results, potentially leading to FDA approval of telaprevir. One study is looking at 12 weeks of telaprevir in combination with standard therapy (peginterferon alfa-2a and ribavirin) followed by either 12 or 36 weeks of standard therapy alone depending on patients' response to therapy. A second study is comparing 8-week and 12-week regimens of telaprevir in combination with standard therapies followed by at least 12 weeks of standard therapy, depending on patients' response

to therapy, to a placebo group taking 48 weeks of standard therapy alone. Both studies are currently closed to recruitment.

Hepatitis C

Hepatitis C is a contagious liver disease that ranges in severity from a mild illness lasting a few weeks to a serious, lifelong illness that attacks the liver. It results from infection with the hepatitis C virus (HCV), which is spread primarily through contact with the blood of an infected person. HCV is a serious public health concern, affecting 3.4 million individuals in the United States. There are six major genotypes of the hepatitis C virus, which are indicated numerically. About 70 percent of hepatitis C patients in the United States have genotype 1. Though many people with HCV infection may not experience symptoms, others may have symptoms such as jaundice, abdominal pain, fatigue and fever. Chronic HCV significantly increases a person's risk for developing long-term infection, chronic liver disease, cirrhosis or death. It is the leading reason for liver transplantation in the United States. Co-infection with HIV is common and rates among HIV positive populations are higher. Most people become infected with the hepatitis C virus by sharing needles or other equipment to inject drugs.

Source: New York- Presbyterian Hospital (news : web)